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Optimizing Chronic Pain Management

with

Duragesic®

FENTANYL TRANSDERMAL SYSTEM

Janssen Pharmaceutica Products, L.P.

Duragesic® Patient Selection

- A first-line choice for:
  - Patients with chronic, moderate–to-severe pain who cannot be managed by lesser means such as acetaminophen-opioid combinations, nonsteroidal analgesics, or as-needed dosing with short-acting opioids
  - Patients who require around-the-clock opioids

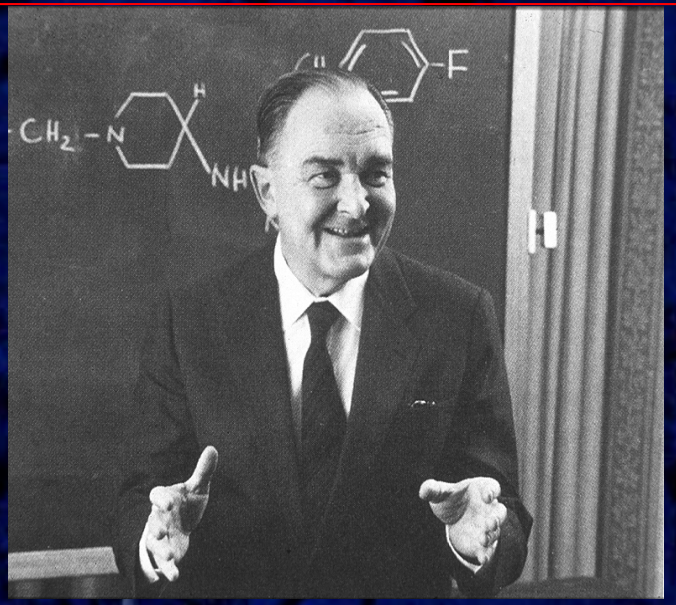
(Adapted from Duragesic PI, 2001)

Duragesic® Contraindications

- Because serious or life-threatening hypoventilation can occur, Duragesic is contraindicated
  - in the management of acute or postoperative pain, including use in outpatient surgeries
  - in the management of mild or intermittent pain responsive to prn or nonopioid therapy
  - in doses exceeding 25 mcg/h at the initiation of opioid therapy in opioid-naïve patients
- Duragesic should not be administered to children under 12 years of age or patients under 18 years of age who weigh less than 50 kg (110 lb) except in an authorized investigational research setting (see Precautions–Pediatric Use)
- The 50, 75, and 100 mcg/h dosages should be used only in patients who are already on and are tolerant of opioid therapy

(Duragesic PI, 2001)

Dr. Paul Janssen, Pain Pioneer



- Dr. Paul Janssen, Belgian physician and prolific researcher, is a pioneer in pain management
- 1953: Janssen Pharmaceutica founded with a mission to develop new medicines, particularly analgesics
- 1960: Fentanyl developed by Dr. Janssen
- 1983: Transdermal delivery systems developed
- 1991: Duragesic® launched, delivering the potency of fentanyl analgesia through slow, safe transdermal delivery

(Schwartz, 1989)

Advantages of Fentanyl in the Duragesic® Patch

Science	Clinical Significance
Fentanyl is a small, lipophilic molecule[1]	Able to pass through patch release membrane and form a depot in skin[1] Fentanyl passes readily across the blood-CNS barrier[1]
Fentanyl is 75 – 100 times more potent than morphine[1]	Only microgram amounts of fentanyl is needed for analgesia[1]
Fentanyl has no active metabolites in contrast to other opioids[1]	No active metabolites to accumulate with chronic dosing Oxycodone and morphine sulfate have active metabolites that may accumulate with chronic dosing
Fentanyl transdermal patch bypasses the GI tract	Favorable side-effect profile[2]

(1. Jeal, 1997; 2. Slappendel, 1994; 3. OxyContin PI, 2001; 4. MS Contin PI, 2000)

Fentanyl Metabolism

Science	Clinical Significance
Fentanyl has no active metabolites in contrast to other opioids[1]	No active metabolites to accumulate with chronic dosing Oxycodone and morphine sulfate metabolites may accumulate with chronic dosing
Fentanyl is metabolized in the liver by the CYP450 3A4 enzyme[1]	Fentanyl is not an inducer or inhibitor of liver enzymes CYP450 3A4 inhibitors (e.g., macrolide antibiotics, azole antifungals and protease inhibitors) may decrease fentanyl clearance rate, so patients should be monitored and dose adjusted if necessary[2] Fentanyl does not interfere with drugs requiring CYP450 2D6 metabolism (e.g., SSRIs, quinine). Oxycodone requires CYP450 2D6 metabolism[3]

(1. Jeal, 1997; 2. Duragesic PI, 2001; 3. OxyContin PI, 2001)

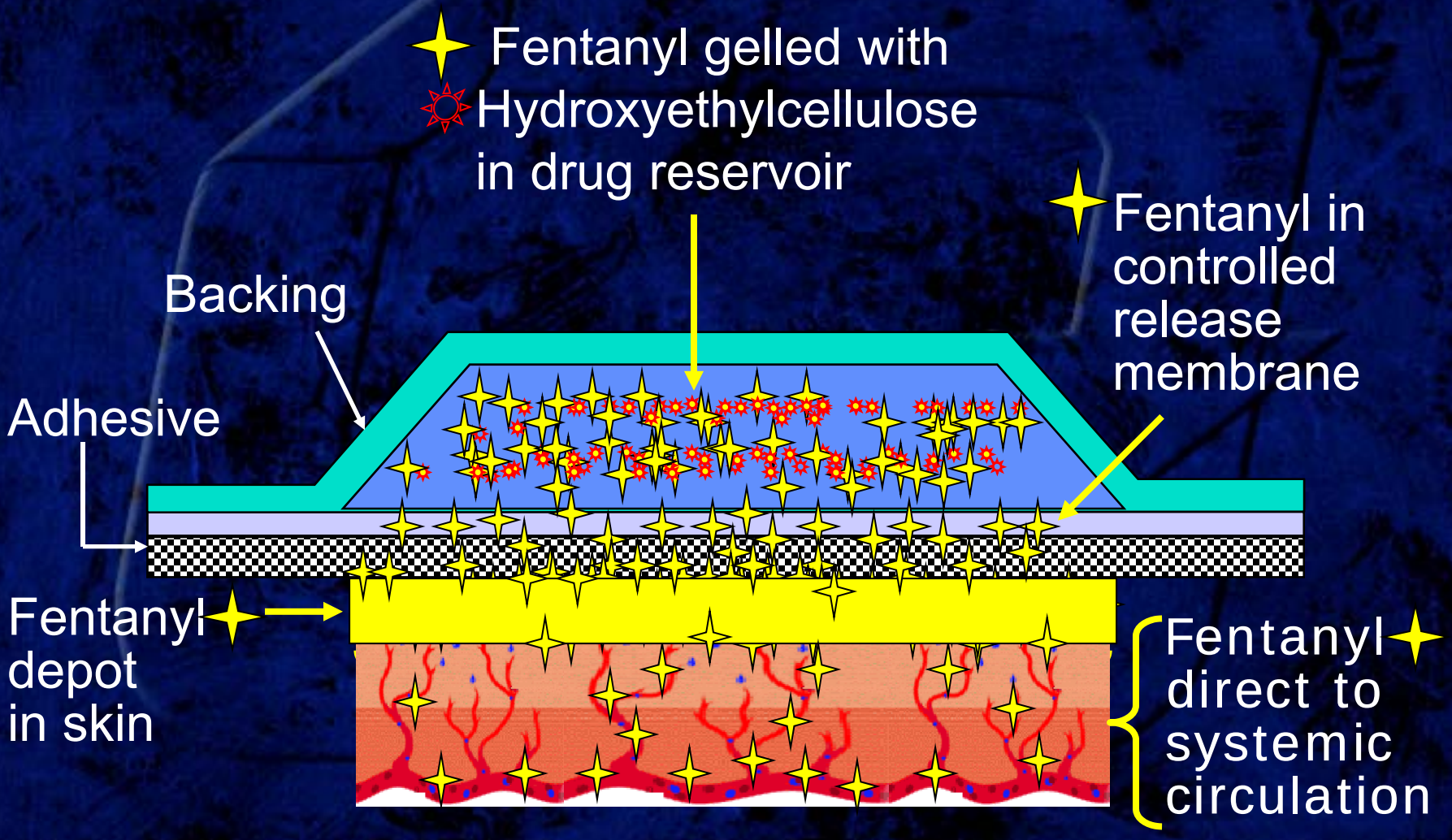
Advantages of Transdermal Delivery

Science	Clinical Significance
Fentanyl depot in upper layers of skin permits sustained, gradual release directly into systemic circulation[1]	Up to 3 days of pain relief[1] Consistent serum levels[1]
Minimizes peaks and troughs, compared to opioids dosed every 4, 6, 8, or 12 hours[1]	Few night-time awakenings[2] Less daytime drowsiness[3] Improved morning vigilance[3]
Fentanyl enters directly into systemic circulation: No GI transit[1] No first-pass metabolism in liver[1]	Improved bioavailability over oral opioid formulations[1] Low incidence of constipation[4]

(1. Jeal, 1997; 2. Simpson, 1997; 3. Ahmedzai, 1994; 4. Slappendel, 1994)

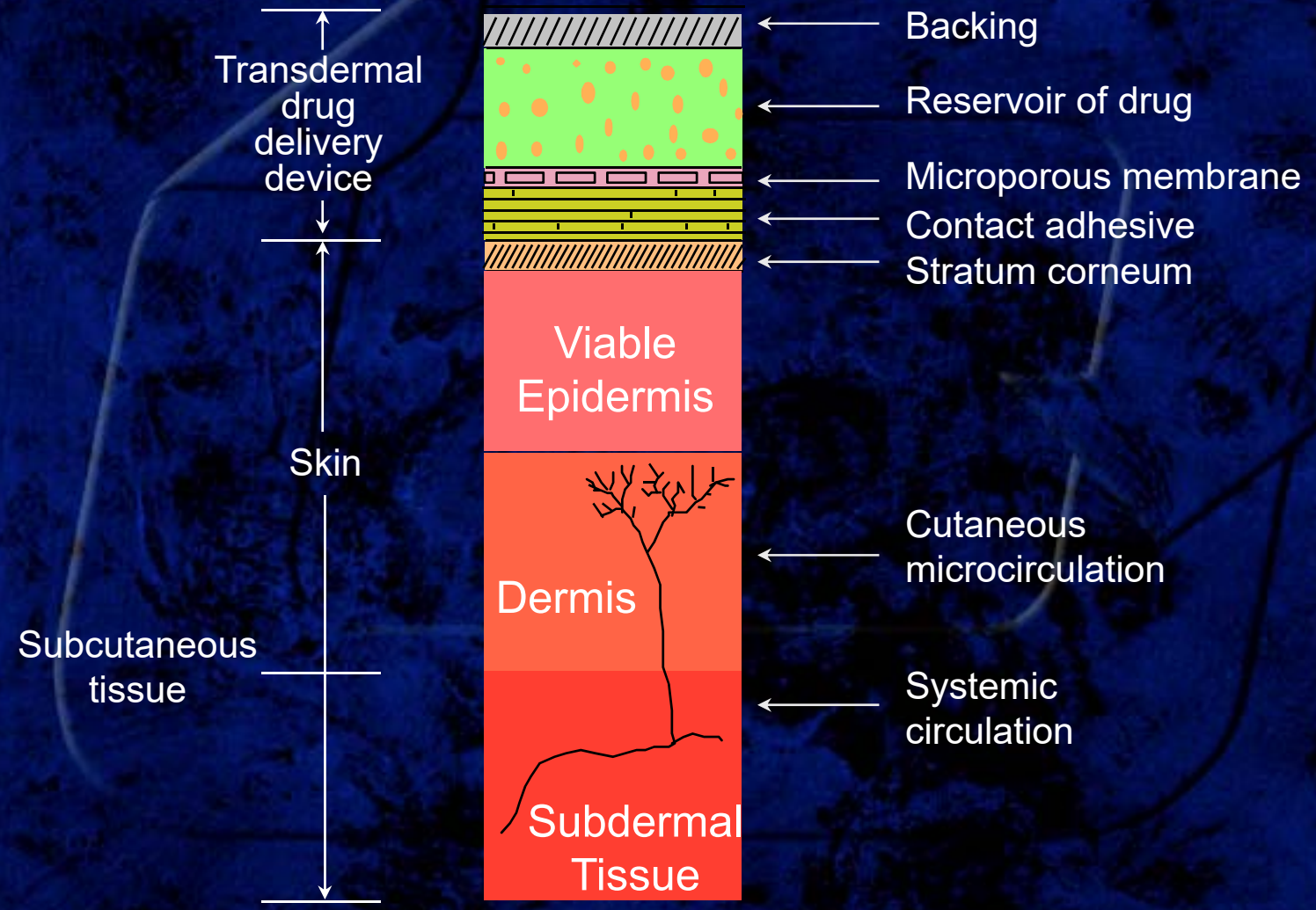
Duragesic®: Fentanyl Transdermal System

Delivers fentanyl direct to circulation



(Adapted from 1. Jeal, 1997; 2. Southam, 1995)

Pathway for Fentanyl Absorption



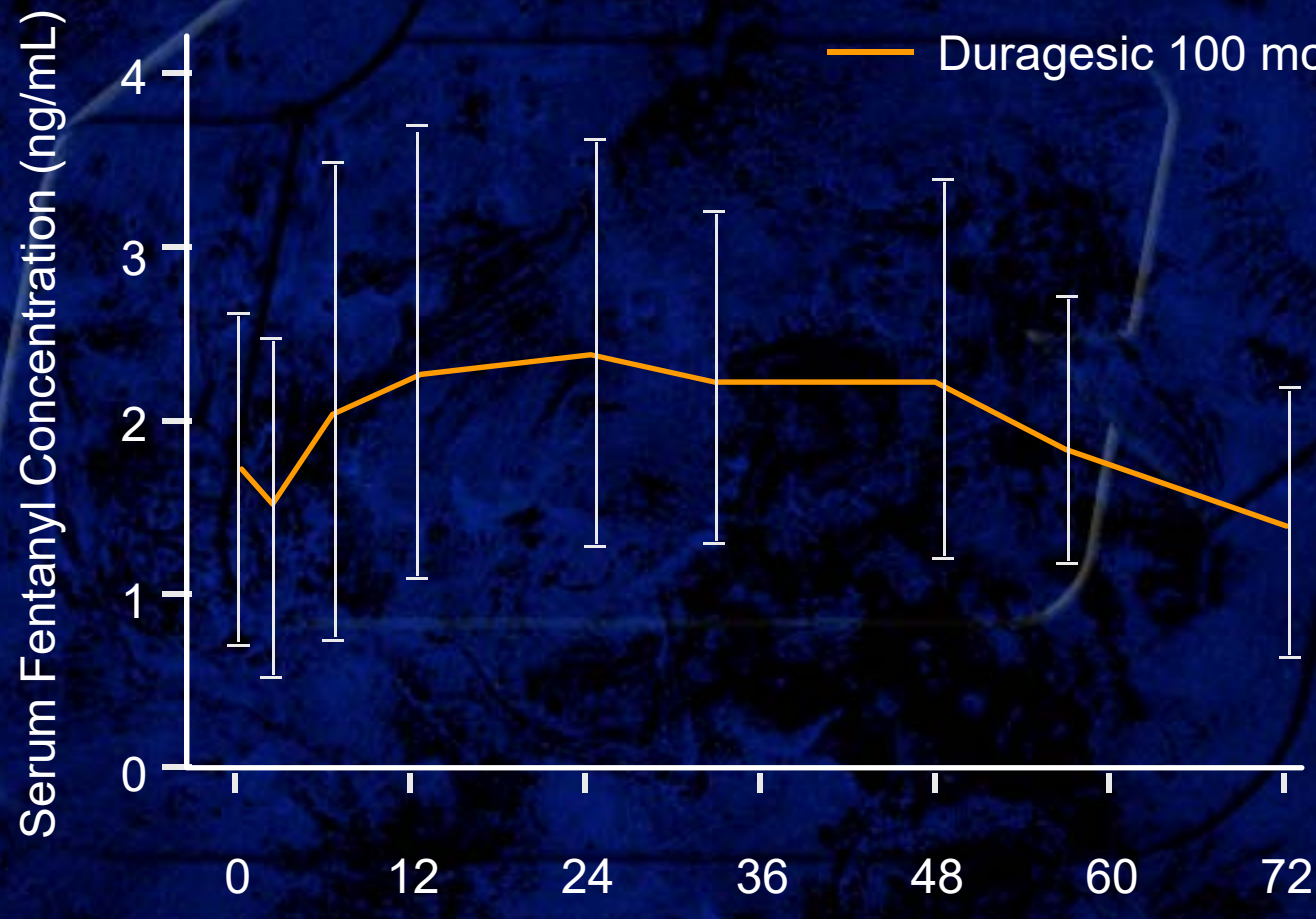
(1. Varvel JR 1989; 2. Jeal W, 1997)

Pharmacokinetics of Duragesic®

Duration of action 72 hours Some patients require 48-hour dosing[1]	Half-life Approximately 17 hours[1] Allows serum drug level to remain steady while patches are changed
Peak serum concentrations 24-72 hours[1]	Steady-state After several sequential patch applications[1]
Onset of action Serum levels increase gradually, leveling off between 12 and 24 hours[1]	Metabolized in liver primarily to norfentanyl (inactive metabolite)[2] Primarily renal excretion[1]

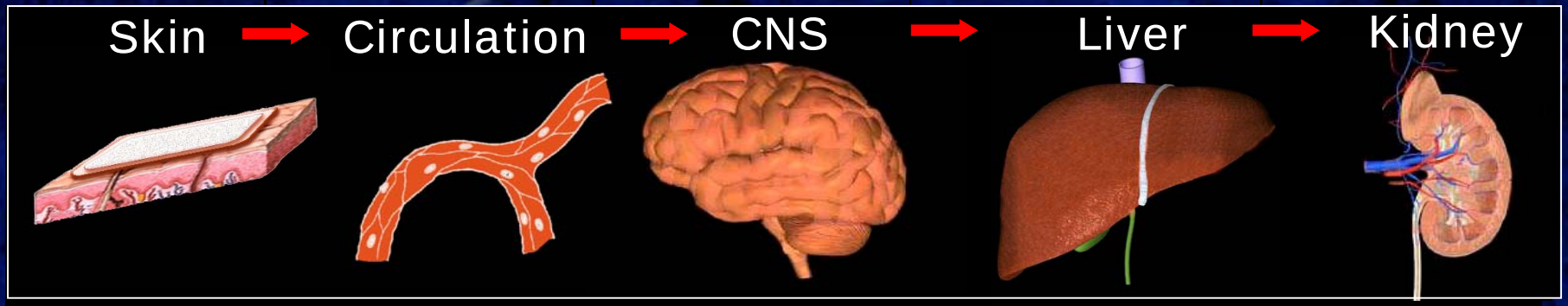
(1. Duragesic PI, 2001; 2. Jeal, 1997)

Steady-State Mean Serum Concentrations for 72 Hrs After Multiple DURAGESIC® 100 mcg/h Applications



(Southam, 1995)

Duragesic®: Metabolism and Effects



Feature				
Fentanyl absorbed from patch into skin; slowly released into circulation[1]	Fentanyl enters circulation directly; by passes GI tract[1]	Fentanyl passes readily through blood-CNS barrier. Fentanyl is a pure mu receptor agonist[2]	No first-pass liver metabolism[1]	Inactive metabolites eliminated by kidney[3]
Clinical Significance				
Up to 72 hours of pain relief ; minimizes peaks and troughs[1]	Low incidence of constipation (14%)[2]	Few side effects associated with interactions with other receptors [2]	No accumulation of active metabolites	

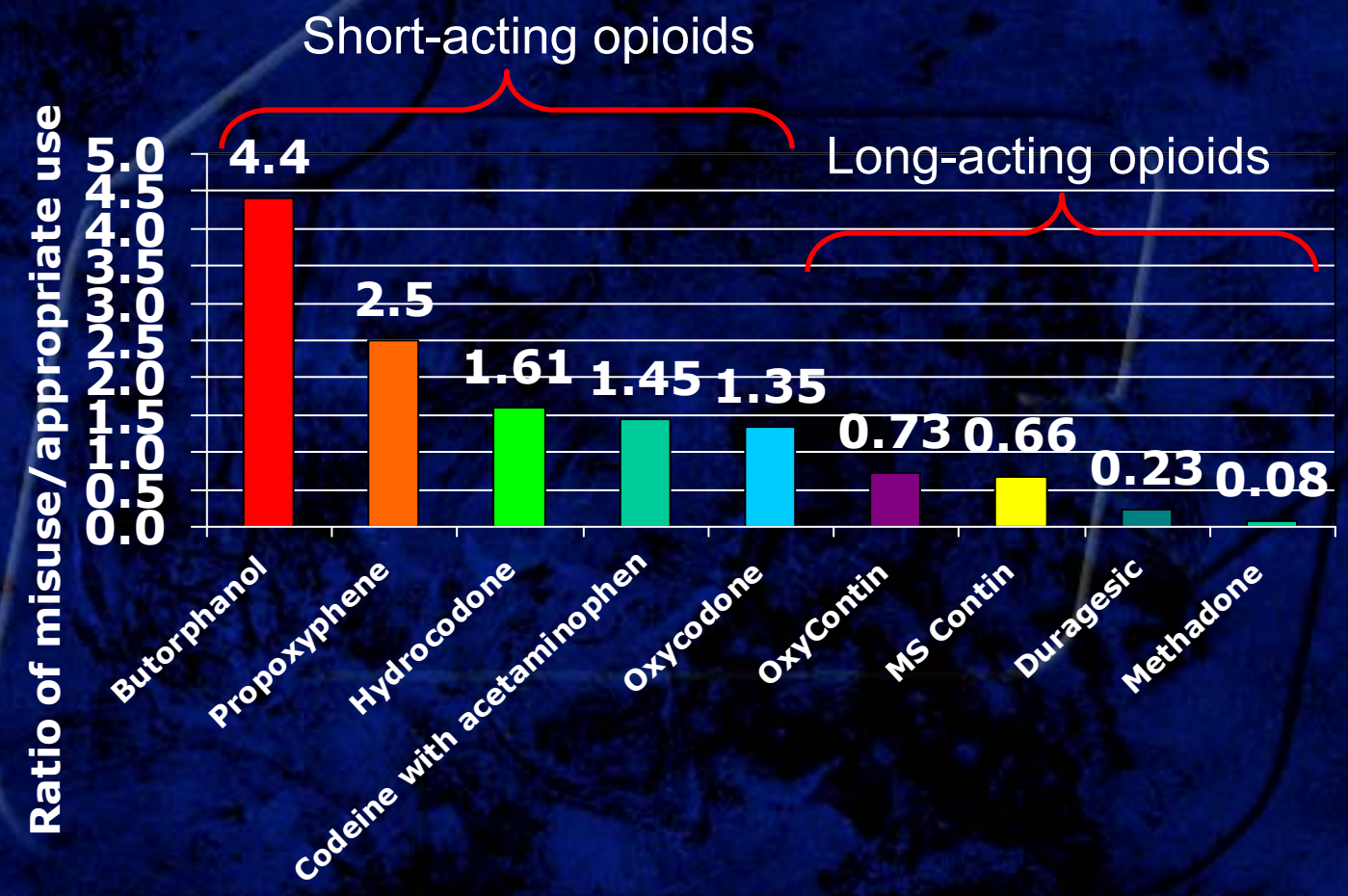
(1. Southam, 1995; 2. Jeal, 1997; 3. Duragesic PI, 2001)

Drug Delivery Systems And Abuse

- Route of administration and rate of action affect abuse potential[1]
- Rapid action gives strong effect and raises abuse liability
  - Smoked or injected drugs reach the brain rapidly[1]
  - "Crushed or chewed sustained release tablets will release all their contents at once, resulting in a risk of fatal overdose"[2]
  - Transdermal delivery produces gradual absorption and clearance,[3] drug takes longer to reach the brain

(1. Mathias, 1997; 2. OxyContin PI, 2000; 3. Jeal, 1997.)

Misuse Potential of Opioids: A 3-Year Retrospective Review



(Mironer, 2000)

Opioid Mentions in Drug Abuse Warning Network (DAWN) Reports, 1990-96

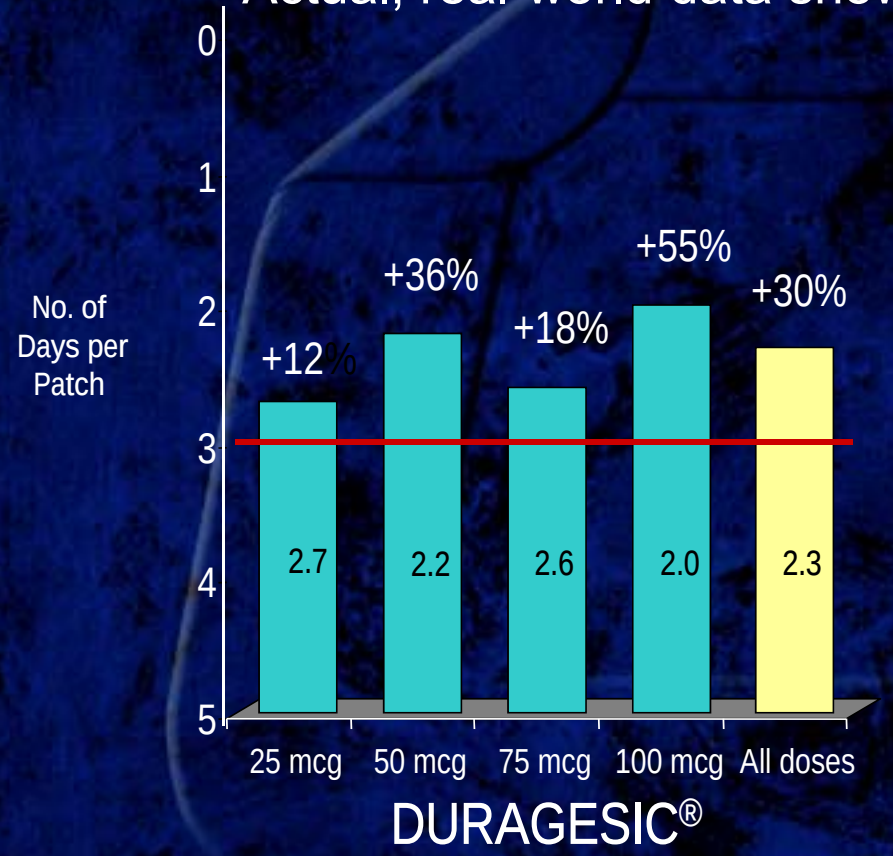
DAWN recorded illicit drug-use incidents resulting in ER Visits at ~500 Urban Hospitals

- Opioids surveyed: fentanyl (all formulations), hydromorphone, meperidine, morphine, oxycodone
- Opioids accounted for <4% of total DAWN mentions
- Opioid drug mentions decreased by 25% from 1990 to 1996
- Year 2000 update shows increase in oxycodone mentions to 10,800 (1.8% of total) compared to 291 fentanyl mentions (.05% of total)

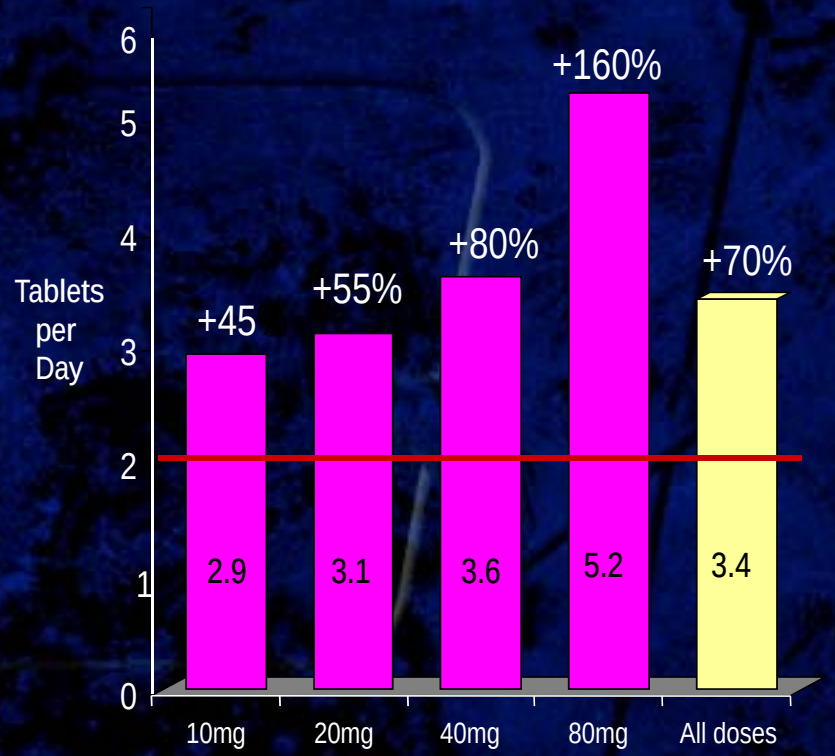
(Joranson DE, 2000; DAWN, 2000)

Medi-Cal Retrospective Database Review

Actual, real-world data shows higher prescriptions relative to PI



DURAGESIC®



OxyContin®

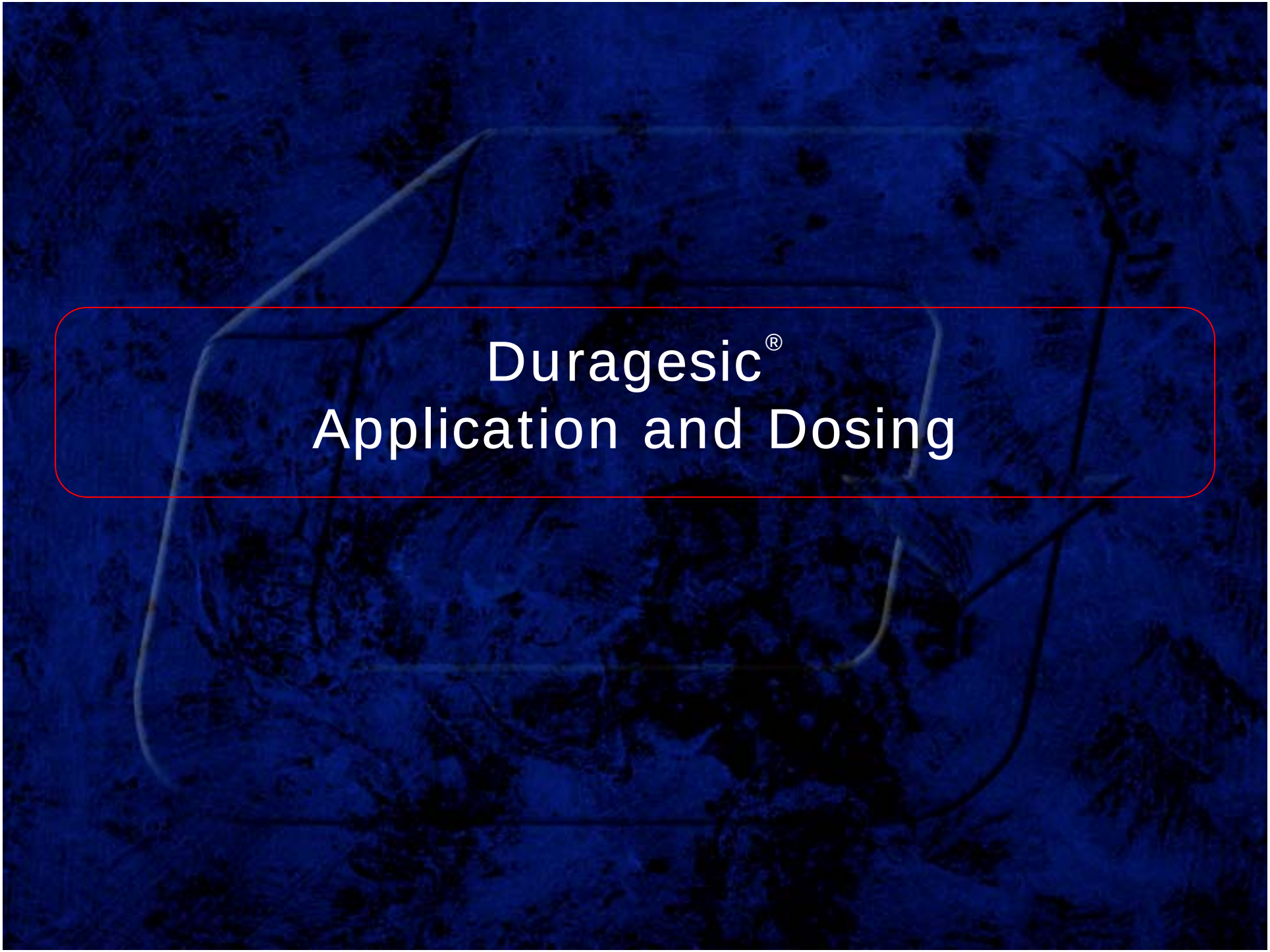
* Based on 98,344 Medi-Cal prescriptions for malignant or nonmalignant pain between January 1, 1997, and August 31, 1999. Percentage difference between actual and recommended number of units per day is shown above the bars.

(Malkin JD, In press)

Red line indicates PI recommendation.

Duragesic® Benefits: Summary

- Long duration of action (up to 3 days)
- Around-the-clock analgesia
- Opioid absorbed directly into circulation, no gastrointestinal transit, no first pass through liver
  - —Favorable side-effect profile
  - —Low incidence of constipation
  - —No active metabolites
- In 10 years of use, low and stable reported rate of abuse


Duragesic®
Application and Dosing

Duragesic®: A First-Line Choice for Chronic Around-the-Clock Opioid Therapy

- Consider as first-line for patients with moderate-to-severe chronic pain who require continuous opioid analgesia:
- Degenerative joint disease[1]
  - Chronic back pain[1,2]
  - Cancer pain[4,5,6]
  - Has been shown to be effective in certain cases of chronic neuropathic pain[2,3]

(1. Allan, 2001; 2. Rowbotham, 1999; 3. Dellemijn, 1997; 4. Payne, 1998; 5. Ahmedzai, 1997; 6. Duragesic PI, 2001)

4-Step Duragesic® Dosing Algorithm

1. Determine appropriate Duragesic starting dose
2. Anticipate and manage side effects
3. Treat breakthrough pain; individualize therapy by titrating to pain relief
4. Monitor need for dose increase

Step 1:
Determine Duragesic® Starting Dose

- Calculate total daily dose of previously used opioid
- Use Duragesic dosage calculator or charts on following slides to convert to corresponding Duragesic dose
- Use no greater than 25 mcg/h in opioid-naïve patients
- Prescribe a short-acting opioid for possible breakthrough pain

(Adapted from Duragesic PI, 2001)

Starting Duragesic®

- During initial application, prescribe a short-acting analgesic for pain coverage until analgesic efficacy with Duragesic is attained
- Initial dose may be increased after 3 days
- Allow approximately 6 days (2 patch applications) for serum levels to reach steady state before making further dose increases
- Do not use doses greater than 25mcg/h in elderly, cachetic, or debilitated patients, unless they are already taking more than 135 mg/d of oral morphine or the equivalent of another opioid

(Duragesic PI, 2001)

Duragesic® Starting Dose Conversion Chart

Prior Regimen	Duragesic Regimen
Fixed-combination short-acting opioids (6/day): –Lorcet 5 mg/500 mg –Lortab 5 mg/500 mg –Percocet 5 mg/325 mg –Percodan 5 mg/325 mg –Tylenol + Codeine 30 mg/325 mg –Tylox 5 mg/500 mg –Vicodin 5 mg/500 mg	One 25 mcg/h Duragesic patch once every 3 days (72 hours)

(Adapted from Duragesic PI, 2001)

Duragesic® Starting Dose Conversion Chart

Prior Regimen	Duragesic Regimen
Long-acting opioids(2/day) OxyContin 20 mg MS Contin 30 mg	One 25 mcg/h Duragesic patch once every 3 days (72 hours)

Multiple patches may be used for doses exceeding 100 mcg/h. Doses up to 6oo mcg/h have been evaluated in clinical trials.

(Adapted from Duragesic PI, 2001)

Goals of Opioid Titration - 1

- Dose titration over time is critical to successful Duragesic therapy
- Gradually increase dose until pain relief is adequate or until unacceptable side effects occur
- A “correct” dose is one that best controls the pain without unacceptable side effects
- Responsiveness of an individual patient to a specific drug varies

(1. Portenoy 1997; 2. Mercadante, 2001)

Goals of Opioid Titration – 2

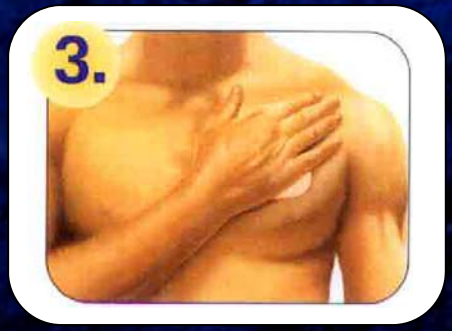
- There is no ceiling dose for opioids. Titrate the dose upward to obtain maximum pain relief without unacceptable side effects. Always prescribe rescue medication for breakthrough pain.
- If a patient does not respond well on one opioid, it is important to try another.
- Set the patient's goals and expectations properly at the outset of therapy

(Passik, 1998)

Teach the Three P's of Duragesic® Patch Application

1. <u>PREPARE</u>: Choose a site to apply patch on the chest, back, or any flat part of the body where there is little or no hair. If there is hair, **do not shave (shaving irritates skin).** Instead, clip hair as close to the skin as possible. Clean application site with clear water **only**. **Pat skin completely dry.** Do not apply anything to skin (lotions, oils, etc) before applying the patch

2. <u>PEEL</u>: Peel the liner from the back of the patch



3. <u>PRESS</u>: Patch on skin **with palm of your hand and hold there for a minimum of 30 seconds**, making sure it sticks well, particularly at the edges.

(Duragesic Patient Instructions, 2000)

Step 2:
Anticipate and Manage Side Effects

Problem	Clinical Experience
Nausea/Vomiting	Use antiemetics as needed
Itching	Prescribe antihistamines as needed
Sedation	Tolerance to side effects usually develops within a few days
Constipation	Start a bowel regimen

(1. Brookoff D, 2000; 2. Duragesic PI, 2001)

Adverse Experiences with Duragesic® in Patients with Cancer (n=153)*

Adverse Experience	Incidence	Discontinued
Nausea	23%	6%
Vomiting	22%	3%
Somnolence	17%	2%
Constipation	14%	0%
Diaphoresis	14%	0%
Dry mouth	13%	0%
Confusion	13%	1%
Asthenia	12%	0%
Anorexia	8%	1%
Dizziness	7%	0%
Nervousness	6%	0%

*Patients were also receiving other regimens, including chemotherapy and radiation.
(Adapted from Duragesic PI, 2001)

Step 3: Individualize Treatment: Titrate to Pain Relief Based on Breakthrough Medication Use

Note the amount of breakthrough medication used. If appropriate, titrate Duragesic® according to this chart:

Oral opioid	Breakthrough med used (mg/24h)	Recommended increase
codeine	300	Add 25 mcg/h Duragesic (add patch or change to higher dose patch)
oxycodone	45	
hydrocodone	45	
hydromorphone	12	
morphine	90	

(Adapted from Duragesic PI, 2001)

Step 4: Monitor Need for Dose Increase

- Duragesic® is available in 25, 50*, 75*, and 100* mcg/h dose strength
- Multiple patches may be used for doses exceeding 100 mcg/h (doses up to 600 mcg/h have been administered in clinical trials)

1. Duragesic should be prescribed every 72 hours
2. If pain relief is insufficient or declines before 72 hours, an increase in dose should be evaluated before using 48-hour dosing

   - A small number of patients may require 48-hour dosing

*For use in opioid-tolerant patients only.
(Duragesic PI, 2001)

Duragesic® : Troubleshooting Problems

Patch loosens	Press in place for at least 30 seconds Secure patch with first-aid tape
Patch falls off	Immediately replace with a NEW patch on new skin site; replace new patch in 3 days
Patient requires more than 100 mcg/h	Use multiple patches; doses up to 600 mcg/h have been used in clinical trials
Pain relief declines before 72 hours	First evaluate increased dose, then consider 48-hour dosing
Fever	At 104ºF body temperature, absorption may increase by approximately one third; Use with caution in patients with fever; Dose should be adjusted if necessary
Direct heat	Avoid applying direct external heat source to patch (i.e., heating pad, electric blanket) because heat can increase fentanyl uptake

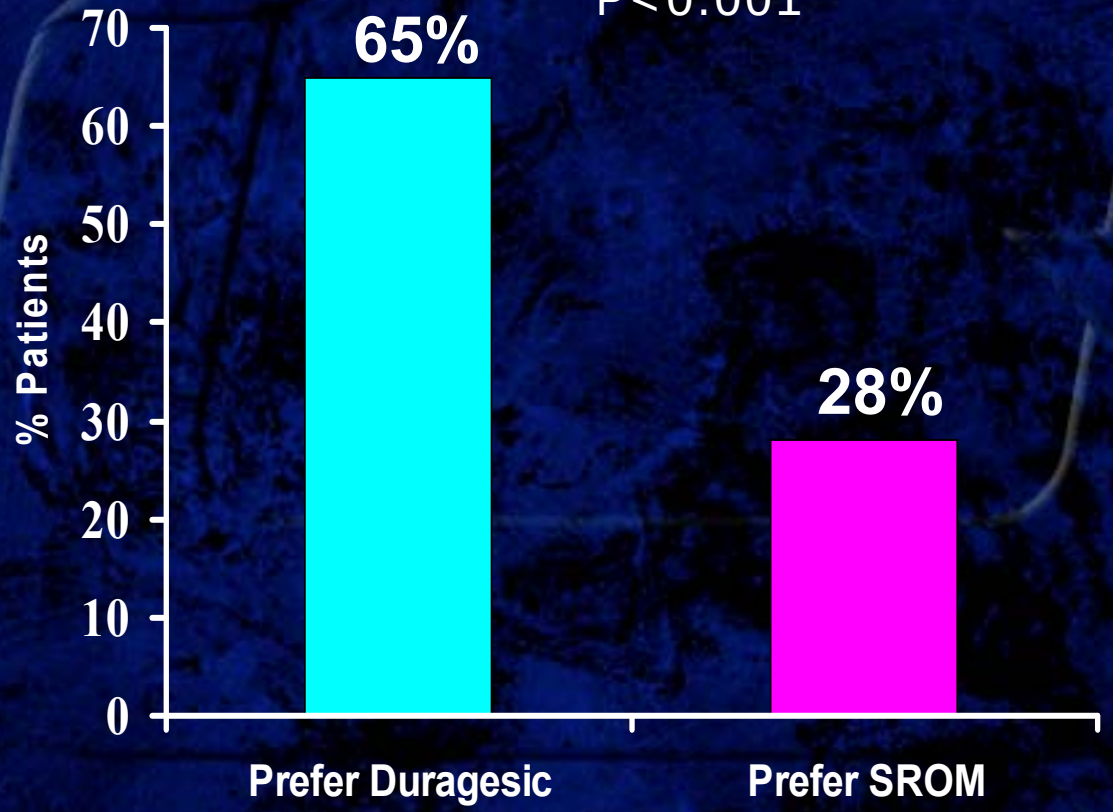
(Duragesic PI, 2001)


Duragesic®
Safety and Efficacy

Duragesic®: Proven Safety and Efficacy

- 11 years of clinical experience since 1991 introduction
- Clinical trial results in malignant and non-malignant pain

Randomised Crossover Trial: Transdermal Fentanyl and Sustained Release Oral Morphine for Treating Chronic Non-Cancer Pain



N=212
non-malignant pain

(Allan, 2001)

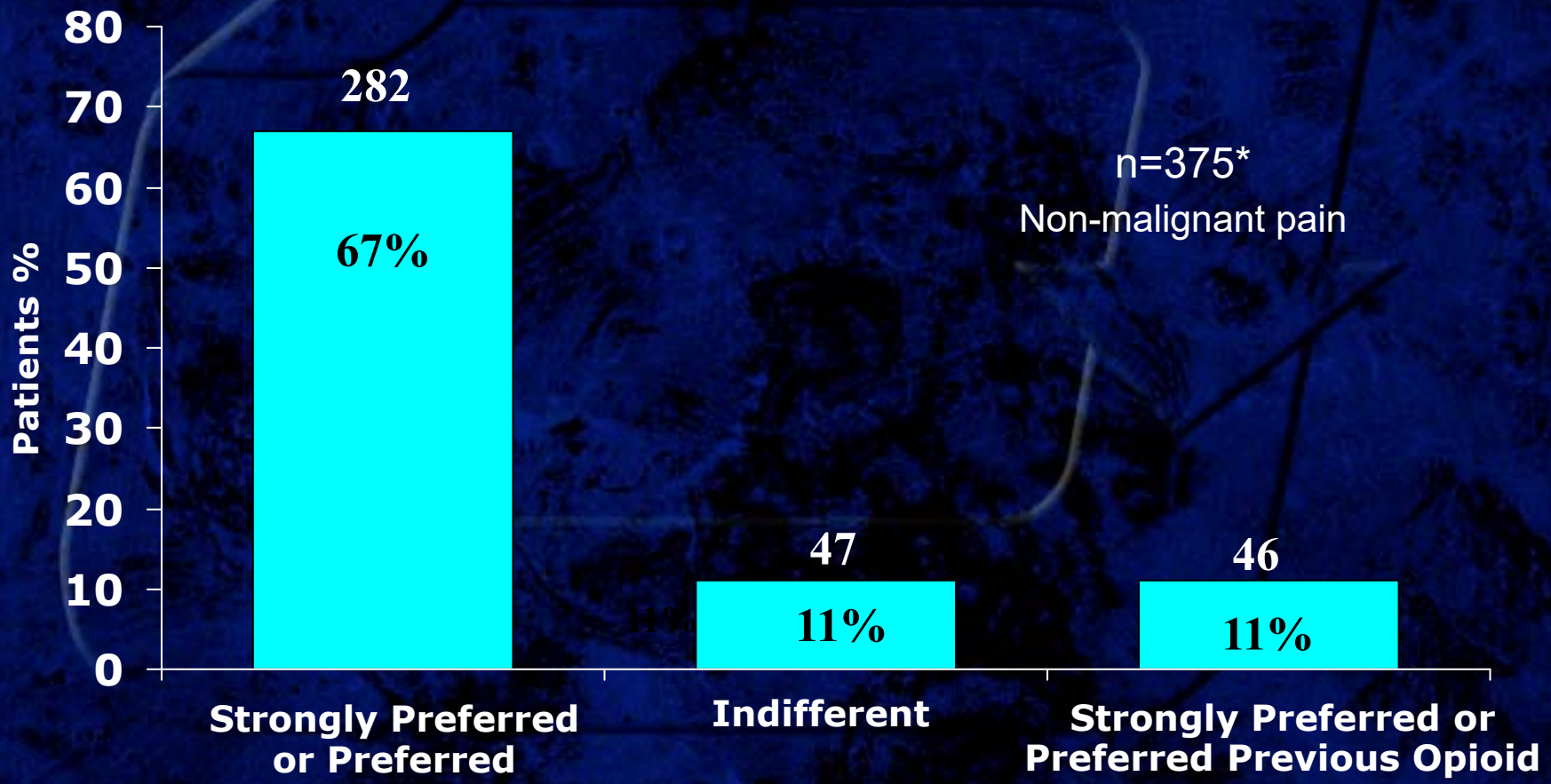
Randomised Crossover Trial: Transdermal Fentanyl and Sustained Release Oral Morphine for Treating Chronic Non-Cancer Pain: Allan, 2001

- Pain Control
  - Duragesic-treated patients had lower mean pain intensity scores than those treated with sustained release morphine ($p<0.001$)
  - More patients treated with Duragesic considered their pain control to be "good" or "very good" (35% vs 23%, $p=0.002$)
  - Global efficacy assessed by patients as "good" or "very good"
    - 60% (Duragesic) vs 36% (SRM), $p<0.001$
  - Investigators' assessed efficacy of fentanyl as "good" or "very good"
    - 58% (Duragesic) vs 33% (SRM), $p<0.0001$

(Allan, 2001)

Evaluation of Long-Term Efficacy and Safety: Transdermal Fentanyl in the Treatment of Noncancer Pain: Milligan, 2001

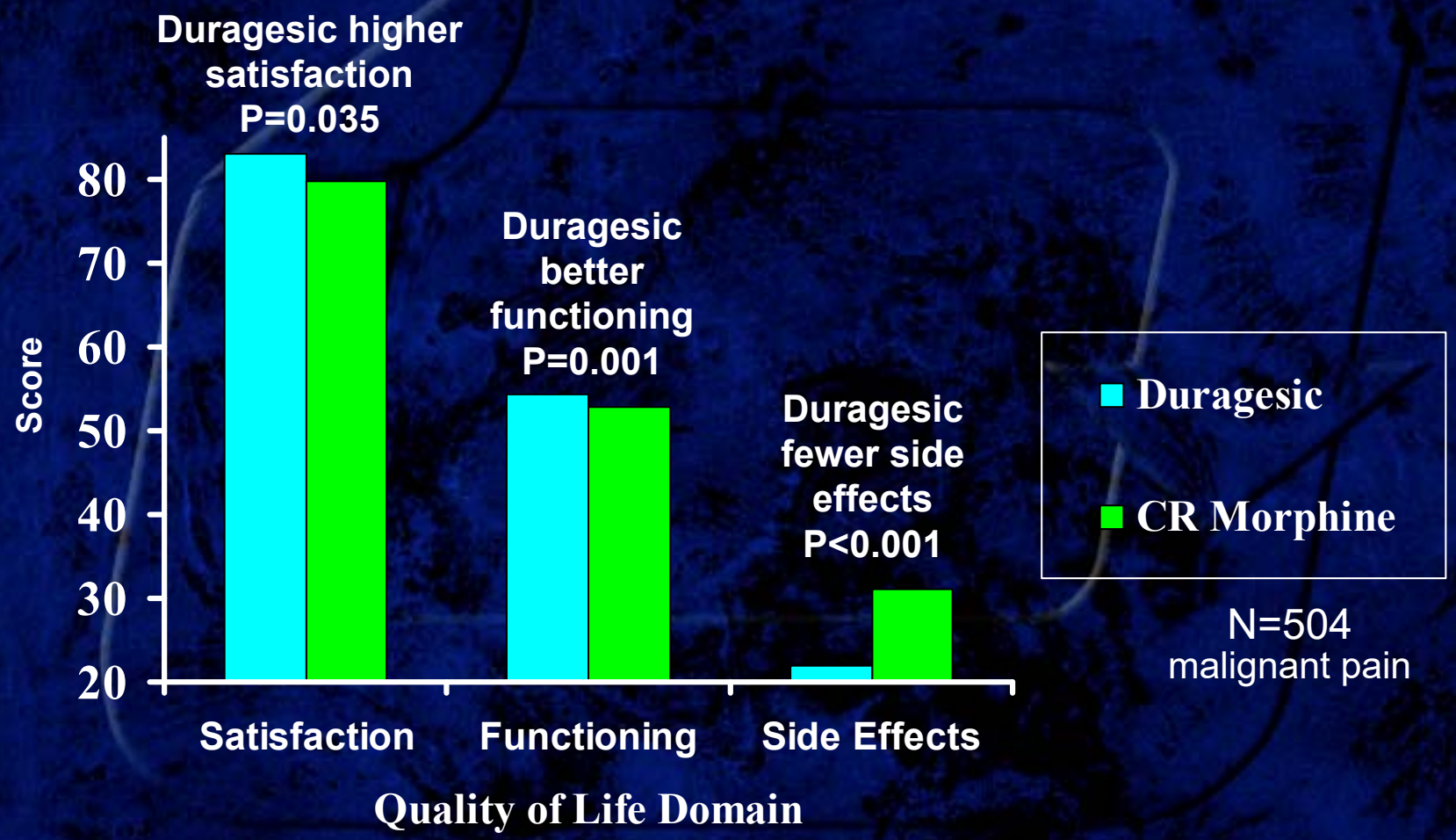
Among chronic Non-Malignant Pain Patients During Months of Duragesic® Therapy (n=421 eligible patients)*



(Milligan, 2001)

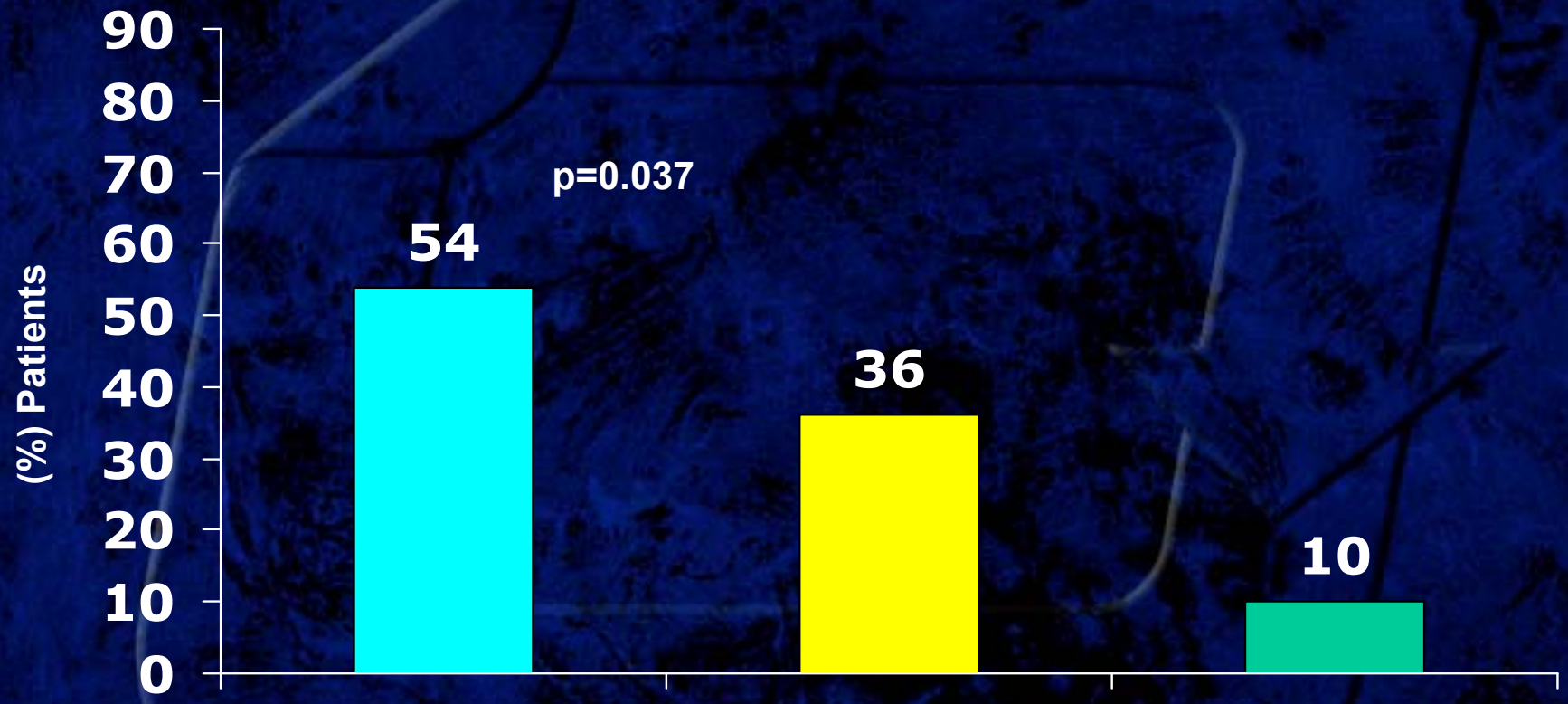
46 patients (11%) did not state preference

Duragesic®: Provides Better Functioning and Fewer Side Effects: Payne, 1998



(Payne R, 1998)

Transdermal Fentanyl versus Sustained-Release Oral Morphine in Cancer Pain: Preference, Efficacy, and Quality of Life: Ahmedzai, 1997



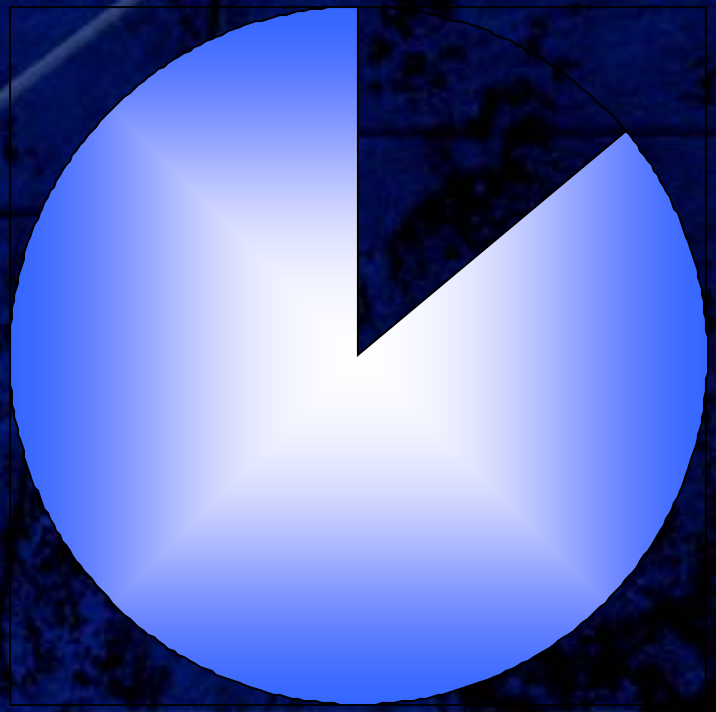
N=136
malignant pain

(Ahmedzai, 1997)

Management of Chronic Pain With Duragesic® in Palliative Home and Hospice Care: 3 Studies

Studies	Demographics	Results
Woodroffe, Hays (1997)	n=48 Ages: 29-82 yrs	80% reported good analgesia 17% discontinued due to nausea
Baumrucker (1996)	2 patient case reports Ages: 50-70 yrs	**Pt 1**: "Good results": "satisfied" with pain regimen; constipation easily treated w/bowel regimen **Pt 2**: "Comfortable"
O'Siorain (1998)	5 patient case reports Ages: 69-89	**Pt 1**: Pain "well-controlled" **Pt 2**: "Excellent" pain relief; no unpleasant adverse effects **Pt 3:** "Well-controlled" pain; "reasonably comfortable" **Pt 4**: Good pain control and well tolerated; eventually discontinued patch for IV morphine **Pt 5**: "Good" pain relief; more alert

Transdermal Fentanyl as Treatment for Low Back Pain



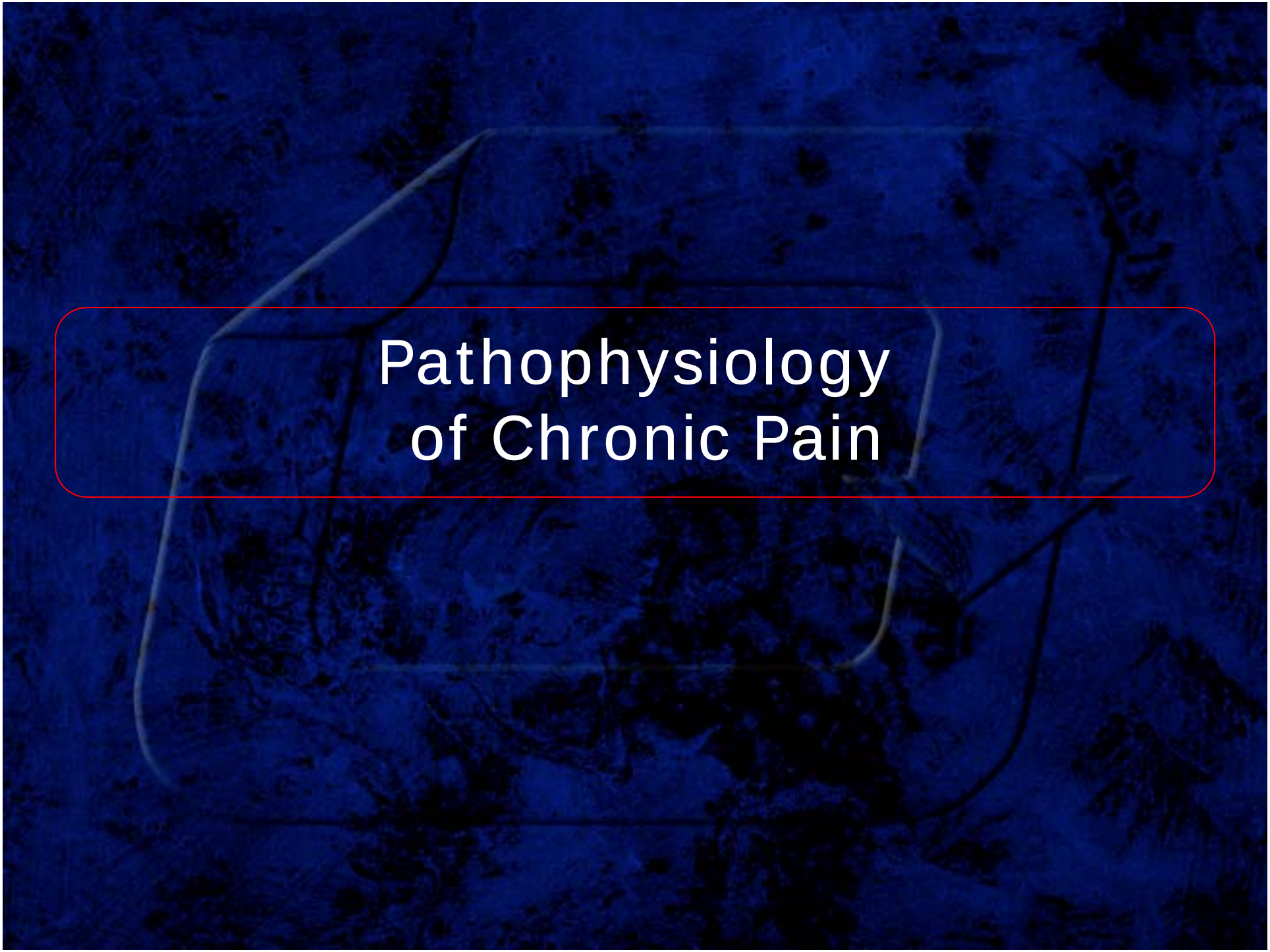
86% of patients experienced overall benefit

- All patients who experienced overall benefit from transdermal fentanyl would recommend it to others with chronic low back pain
- Patients assessed therapy based on parameters of pain control, disability as it related to activities of daily living, and quality of sleep.

(Simpson, 1997)

Duragesic® Delivers Safe, Effective Therapy for Chronic Pain

- Duragesic's duration of action is up to 72 hours
  - Around-the-clock analgesia
  - Minimizes peaks and troughs
- Opioid absorbed directly into circulation, no gastrointestinal transit, no first pass through liver
  - Favorable side-effect profile
  - Low incidence of constipation
  - No active metabolites, fewer drug interactions
  - Consistent serum levels
- In 11 years of use, very rare reports of abuse


Pathophysiology
of Chronic Pain

Pain-Sensing System Malfunction in Chronic Pain

Pain Sensing

In chronic pain, pain signals are generated without physiologic significance

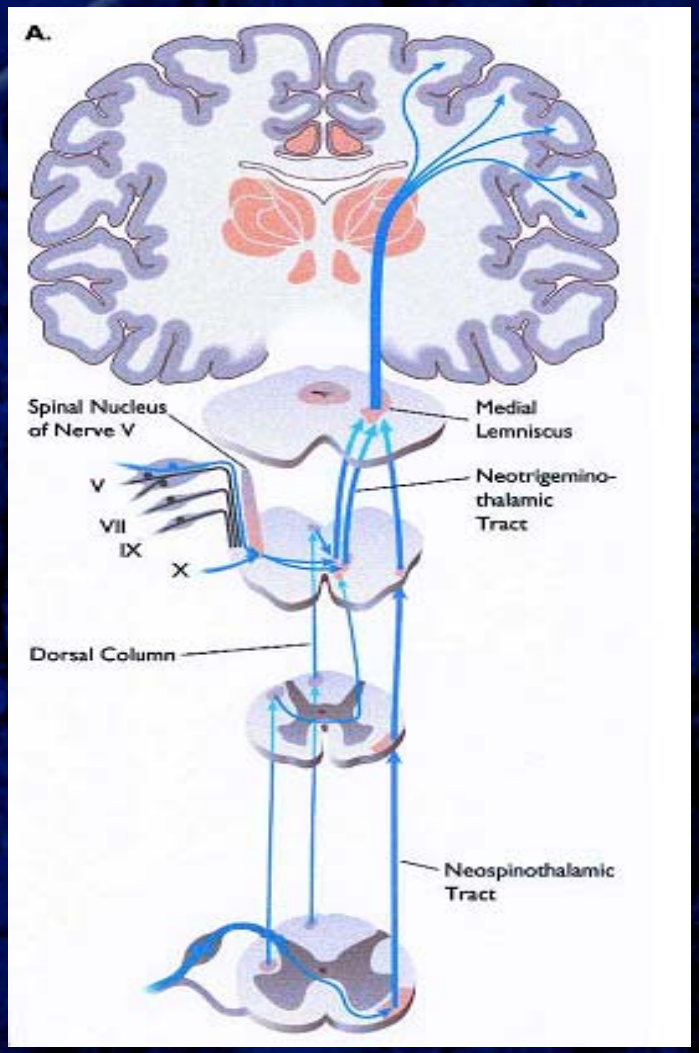
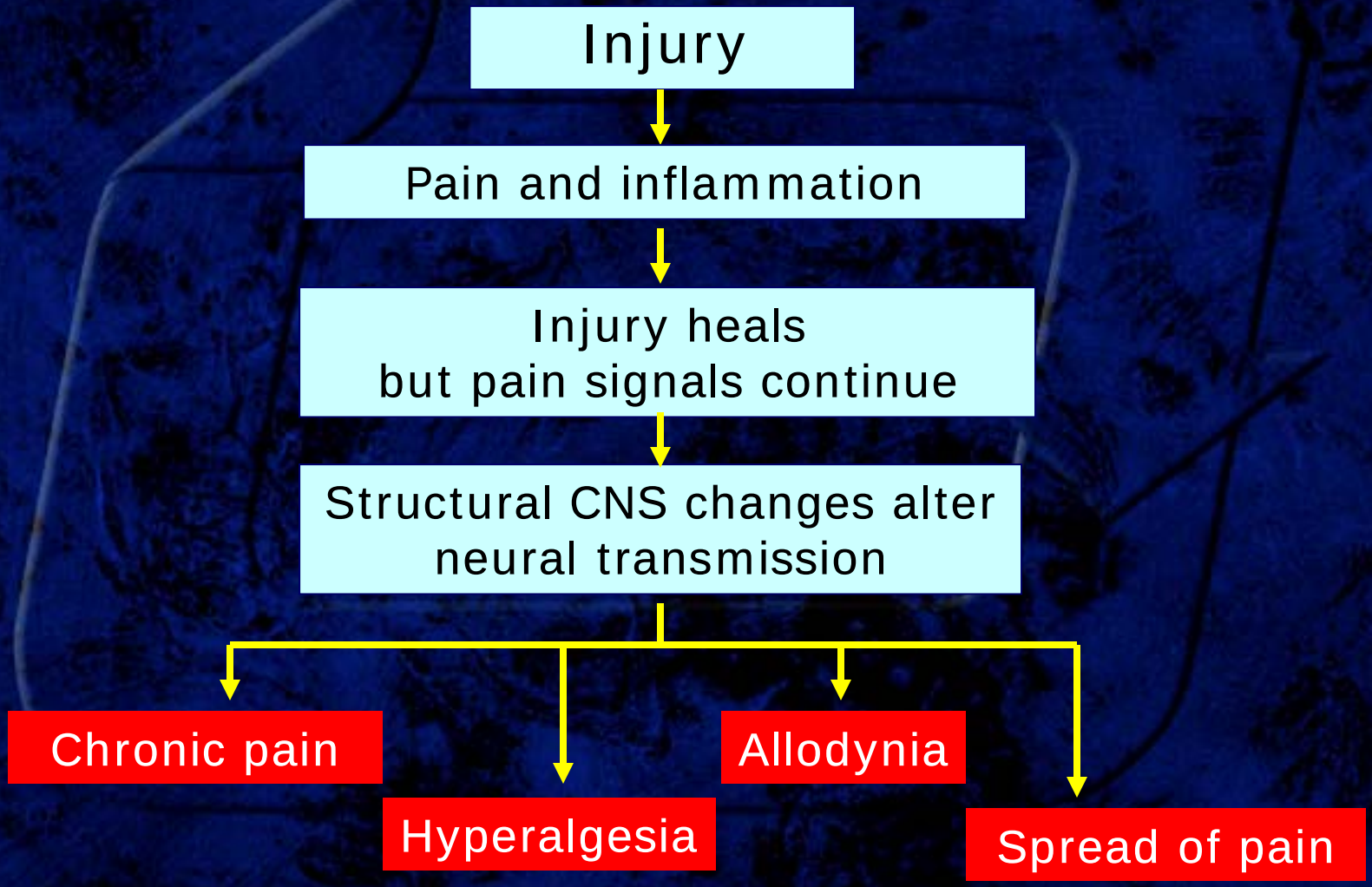


Illustration: Seward Hung

Normal pain:
Pain-sensing signals are initiated in response to a stimulus
- They elicit a pain-relieving response

Chronic pain:
Pain signals are generated for no reason and may be intensified
- Pain-relieving mechanisms may be defective or deactivated

Pathogenesis of Chronic Pain



(Adapted from Marcus, 2000)

Duragesic®, Pain Relief and Opioid Receptors

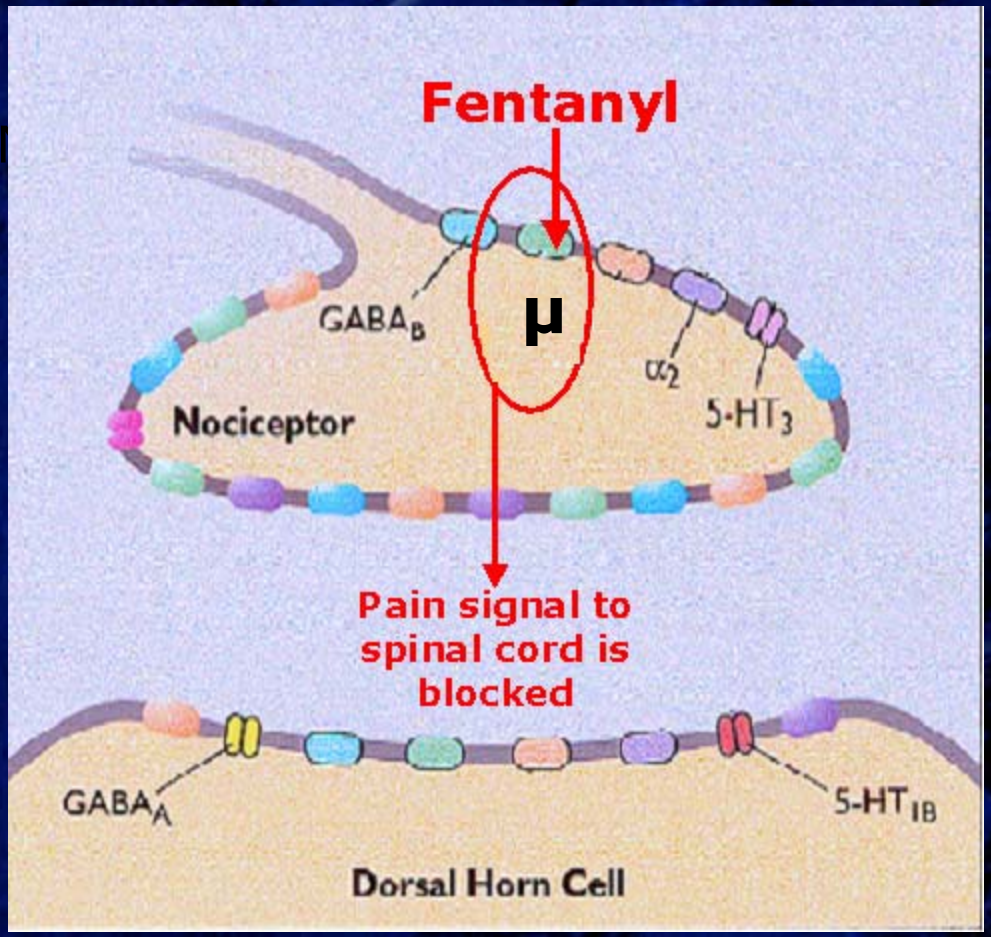


Illustration: Seward Hung

- Fentanyl from the Duragesic patch binds to mu opioid receptors on pain-sensing nerve cells
- Transmission of pain signals to the dorsal horn of the spinal cord is blocked

Chronic Pain Pathophysiology

- The nervous system remodels continuously in response to repeated pain signals
  - Nerves become hypersensitive to pain
  - Nerves become resistant to anti-nociceptive system
- If untreated, pain signals will continue even after injury resolves
- Chronic pain signals become embedded in CNS

(Marcus, 2000)


Guidelines and Prescribing Principles
for Opioid Therapy

Chronic Pain: Prevalence and Impact

- 35% of Americans have chronic pain
- >50 million Americans are partially or totally disabled by chronic pain
- 50 million lost work days per year
- $65 to $75 billion per year cost to society in lost productivity and medical costs

(APS, 1999)

Survey of Chronic Pain in America

In a survey of 805 patients with chronic pain lasting >6 months rated at 5/10, suffering from arthritis, back disorder, other causes:

- 56% had chronic pain for more than 5 years
- 22% were referred to a pain specialist
- 47% changed physicians at least once for one or more of these reasons:
  - Patient experienced “too much pain” (42%)
  - Physician lacked pain-management knowledge (31%)
  - Pain was not taken seriously by physician (29%)
  - Pain was not treated aggressively (27%)
- 14% went to the ER 1+/yr
- 29% switched physicians >3 times

(APS, 1999)

Chronic Pain is Under-Treated Despite Availability of Effective Pain Therapies

- More than a third of patients undergoing therapy for cancer—and 60% to 90% of those with advanced malignancy—report significant pain
- Large segments of the cancer population—in particular, elderly patients in nursing homes, minorities, and women—receive inadequate palliative therapy

(Foley, 2000)

WHO Guidelines for Cancer Pain

- Step 3: Opioids for moderate to severe pain +/- nonopioid +/- adjuvant therapy
- Step 2: Opioids for mild to moderate pain +/- nonopioid +/- adjuvant therapy
- Step 1: Nonopioid +/- adjuvant therapy

(Adapted from Portenoy, 1997)

World Health Organization. Switzerland; 1990.

AAPM/APS Consensus Statement on Opioid Use

The consensus statement on *The Use of Opioids for the Treatment of Chronic Pain*, approved by the American Academy of Pain Medicine and the American Pain Society in 1996, states that "efforts to stop diversion should not interfere with prescribing opioids for pain management." This is consistent with the law and mission of federal and state regulators.

(Amer Acad Pain Med; Amer Pain Soc, 1996)

JCAHO Standards Mandate Pain Management

- The patient's right to pain management is respected and supported.
- The organization plans, supports, and coordinates activities and resources to assure the pain of all individuals is recognized and addressed appropriately. This includes:
  - Initial assessment and regular reassessment of pain
  - Education of relevant providers in pain assessment and management
  - Education of patients, and families when appropriate, regarding their roles in managing pain as well as the potential limitations and side effects of pain treatments
  - Communicating to patients and families that pain management is an important part of care

http://www.jcaho.org/standards_frm.html

Promoting Pain Relief and Preventing Abuse of Pain Medications: A Critical Balancing Act

A Joint Statement from 21 Healthcare Organizations and the Drug Enforcement Agency - October 23, 2001

- Undertreatment of pain is a serious problem in the United States, including pain among patients with chronic conditions and those who are critically ill or near death
- Effective pain management is an integral and important aspect of quality medical care, and pain should be treated aggressively
- For many patients, opioid analgesics – when used as recommended by established pain management guidelines – are the most effective way to treat their pain, and often the only treatment option that provides significant relief

http://www.usdoj.gov/dea/pubs/pressrel/pr102301.html

Physician-Related Barriers to Pain Management

A survey of 897 physicians with patient-care responsibilities in a network of oncology institutions yielded these responses:

- 12% rated their medical school pain education as excellent or good
- 86% believed patients in their practices were undermedicated for pain
- 61% cited reluctance to prescribe opioids as a barrier to pain management in their own practices
- 31% wait until the patient's prognosis is <6 months before prescribing maximal analgesia
- 18% cited concern about "regulatory issues" as a barrier to pain management

(Von Roenn JH, 1993)

The Controlled Substances Act Supports Appropriate Opioid Therapy

- A lawful and valid prescription of a Controlled Substance must be:
  - for a legitimate medical purpose
  - by an individual practitioner
  - in the usual course of professional practice

Adapted from United States Department of Justice: Drug Enforcement Administration: Controlled Substances Act [21 C.F.R. 1306.04(a)].

The FSMB Model Guidelines: Documentation is Your Best Protection

1. Patient Evaluation: Complete medical history/physical exam.
2. Patient Education: On proper use, side effects, risks, benefits.
3. Treatment Plan: Written treatment objectives and plan.
4. Informed Consent & Agreement for Treatment: Written agreement may include urine/serum screenings, number of Rx refills, reasons for discontinuing drug therapy.
5. Monitoring: Treatment compliance, goal attainment.
6. Consultation: Possible referral for additional evaluation and treatment.
7. Medical Records: Accurate and complete records.
8. Comply with the Controlled Substances Laws and Regulations: See DEA *Physician's Manual* and state regulations.

(FSMB of US, 1998)


Implementing the Guidelines for
Opioid Pharmacotherapy

Safe and Effective Duragesic® Prescribing

- Single prescriber takes primary responsibility
  - Working knowledge of published guidelines (WHO, AHCPR, APS)
  - Documentation (tracking prescribing)
- Prescribing principles
  - Patient selection
  - Drug selection
  - Dose to optimal effect
  - Manage side effects
  - Manage the poorly responsive patient
  - Learn principles of addiction medicine sufficient to monitor drug-related behavior and assess aberrant behavior
  - Educate patient and caregiver

(1. WHO, 1997; 2. Jacox, 1994)

Safe and Effective Duragesic® Prescribing

The Goal: To relieve a patient's pain sufficiently to support a return to "life uninterrupted" by chronic pain to the extent possible for that patient

The Process: The Four "A's" of Pain Treatment

1. Analgesia (pain relief)
2. Activities of Daily Living (psychosocial functioning)
3. Adverse effects (side effects)
4. Aberrant drug taking (addiction-related outcomes)

The Result: Document the 4 A's so that your charting defends your prescribing

(Passik & Weinreb, 2000)

Positive Outcomes in Pain Management: Analgesia and Activities of Daily Living

- Document pain status:
  - Use 1 – 10 Numerical Pain Relief Scale (NPS)
  - Visual Analog Scale for Pain Intensity (VAS)
- Set goals related to ADLs:
  - Physical functioning
  - Mood
  - Family relationships
  - Social relationships
  - Sleep patterns
  - Overall functioning
- Document BOTH pain relief and progress toward ADL goals

(Passik, 1998)

Positive Outcomes in Pain Management: Adverse Events

Plan ahead to avoid adverse events and improve pain management outcomes:

- Inform patients about the possibility of side effects and that some may resolve after a few days
- Encourage patients to alert your staff about any uncomfortable side effects
- As with all opioids, patients should be warned about the possibility of respiratory depression

(Passik, 1998)

Issues That Complicate Opioid Prescribing

- Physician-patient agreement
- Fear of iatrogenic addiction
- Differentiating addictive vs other aberrant behaviors
- Management strategies for patients with substance abuse-related problems
- Concern over regulatory scrutiny and ability to identify those who are seeking opioids for non-medical reasons (diversion, sale, recreation)

The Physician-Patient Agreement

- Build trust by using a patient agreement that defines what behaviors constitute responsible drug-taking:
  - Get medicine from only one prescriber and one pharmacy
  - Take medications only as prescribed
  - Refills for lost medicine cannot be given by staff or over the phone but require a visit to the prescribing physician
  - Do not take other non-prescribed medications or share your medications with others
  - Keep all appointments, including those with other professionals (psych, PT, marriage counselor)
  - Set and progress toward goals that improve your life
  - Specify the possibility of random urine screens. If illicit drugs are identified, note that police will be notified

Assess the Risk of Iatrogenic Addiction or Aberrant Behavior in Each Patient

The potential for addiction is in the patient, not the opioid.

~ 45%

HIGH

Long-term exposure to opioids in addicts[2]

<1%

LOW

Short-term exposure to opioids in non-addict[1]

Where is your patient?

(1. Porter, 1980; 2. Dunbar,1996; 3. Adapted from Passik,1998)

Where is Your Patient on the Addiction/Abuse Spectrum?

- Pain treatment plans are based on where your patient is on the addiction potential spectrum
- Addictive behavior occurs in a significant proportion of the US population, which may be reflected in your practice:
  - 6.3% use illicit drugs
  - 3.5% are dependent on illicit drugs
  - 20.6% abuse alcohol (reported binge drinking)
  - 29.3% use cigarettes

(Substance Abuse and Mental Health Services Administration, 2001)

Differential Assessment of Aberrant Behavior

PHYSICAL DEPENDENCE: Pharmacologic effect characteristic of opioids; withdrawal or abstinence syndrome manifest on abrupt discontinuation of medication

TOLERANCE: Pharmacologic effect characteristic of opioids; need to increase dose to achieve the same effect or diminished effect from same dose

PSEUDO-ADDICTION: Pattern of drug-seeking behavior of pain patients receiving inadequate pain management that can be mistaken for addiction; resolves with reestablishing analgesia

ADDICTION: A chronic, relapsing condition resulting from many complicated influences including chemical, genetic, familial and social factors

CHEMICAL COPING: Behavior bears a resemblance to addiction because pill-taking is inappropriately used to manage stress

(1. Portenoy, 1997; 2. Weissman, 1989)

Behaviors That Raise Suspicion of Addiction/Abuse

Probably more predictive

- Selling prescription drugs
- Prescription forgery
- Stealing or borrowing another patient's drugs
- Injecting oral formulation
- Obtaining prescription drugs from non-medical sources
- Concurrent abuse of related illicit drugs
- Multiple unsanctioned dose escalations
- Recurrent prescription losses

(Portenoy, 1997)

Probably less predictive

- Aggressive complaining about need for higher doses
- Drug hoarding during periods of reduced symptoms
- Requesting specific drugs
- Acquisition of similar drugs from other medical sources
- Unsanctioned dose escalation 1 – 2 times
- Unapproved use of the drug to treat another symptom
- Reporting psychic effects not intended by the clinician

Treatment Plans To Reduce Risk in Patients With Higher Abuse Potential

- Select opioids with lower abuse potential
- Have patients sign written contracts
  - –Use contract as a teaching tool, informed consent
- Schedule frequent clinic visits
- Prescribe small quantities of medications
- Renew prescriptions contingent upon clinic attendance
- Use 12-step programs where possible
- Consider urine toxicology screens
- Involve family in treatment planning
- Document all concerns
- Refer to addiction specialist

Protect Your Practice: Use the Guidelines

- JCAHO: Joint Commission on the Accreditation of Healthcare Organizations www.jcaho.org
- APS/AAPM: American Pain Society/American Academy of Pain Medicine www.ampainsoc.org
- NCCN: National Cancer Care Network www.nccn.org
- WHO: World Health Organization www.who.int
- FSMB: Federation of State Medical Boards of US www.fsmb.org
- DEA www.usdoj.gov
- Federation of State Medical Boards of the US www.fsmb.org
- Pain & Policy Studies Group, University of Wisconsin – State regulations www.medsch.wisc.edu/painpolicy

Summary: Opioid Prescribing Principles

- When prescribing Duragesic® for chronic pain, follow established principles and guidelines for opioid prescribing
- Monitor and document the Four A's
- Be alert for the signs of the rare drug abuser or diverter
- Seek consultation when appropriate